

a.) Amendments to the Specification

Please insert the following new paragraph on page 1 after line 2, before line 3.

This application is a division of application No. 09/269,576 filed March 30, 1999, which is in turn a §371 of PCT/JP97/03442 filed September 26, 1997, which claims priority benefit of JP 8-259432 filed September 30, 1996, the subject matter of each of which is incorporated by reference herein.

Please amend the paragraph starting at page 1, line 12 and ending at page 2, line 13 to read as follows (the changes are indicated in bold):

E2F is a transcription factor of importance for the transcription of a great number of genes involved in the progress of cell cycle and serves as a target protein of tumor suppression gene product Rb [EMBO J., 9, 2179 (1990); Cell, 65, 1053 (1991)]. As proteins comprising E2F, E2F family and DP family have been known. Up to now, five molecules of the E2F family, namely E2F 1 to 5 have been identified, while two molecules of the DP family, namely DP1 and 2, have also been identified. It has been believed that **the** out of control **of the** expression or activity of E2F is deeply involved in the carcinogenesis of a great number of cells [Science, 258, 424 (1992); Trends in Biological Chemistry Science, 19, 108 (1994)]. It has also been reported that the inhibition of the transcriptional activity of E2F can suppress the growth of smooth muscle cells, which works as the cause of arteriosclerosis [Proc. Natl. Acad. Sci. USA., 92, 5855 (1995)]. Thus, the substance suppressing the E2F activity is useful as a therapeutic agent of tumor or diseases involving the abnormal growth of smooth muscle cells or the like, such as arteriosclerosis. Additionally, the substance may also be effective widely for autoimmune diseases which are exacerbated due to the growth of synovial cell, such as chronic

rheumatoid arthritis, or diseases occurring because of the abnormal growth of mesangium cell, such as nephropathy. As to E2F suppressing agents, nucleic acid based compounds have been known, including antisense RNA [Cancer Res., 54, 1402 (1994)] and decoy based on the E2F binding sequence DNA [Proc. Natl. Acad. Sci. USA., 92, 5855 (1995)]. However, no peptides have been known yet as such suppressing agents.

Please amend the paragraph at page 4, lines 3-9 to read as follows:

The heteroaryl moiety of the heteroarylcarbonyl and the heteroaryloxycarbonyl includes e.g., furyl, thienyl, pyridyl, ~~pyrazolyl~~, pyrazolyl, pyrazolyl, pyrimidinyl, pyradinyl, indolyl, quinolyl, isoquinolyl, and quinazolyl. Each of the substituted heteroarylcarbonyl and the substituted heteroaryloxycarbonyl has the same substituents as defined for the substituents of the substituted aroyl.

Please amend the paragraph at page 5, lines 13-16 to read as follows:

The peptide sequence comprising a partial amino acid sequence having at least 12 continuous residues in the sequence of the dimerization region of the E2F includes SEQ ID NO:25, e.g., a sequence represented by the general formula (Ia);

Please amend the paragraph starting at page 5, line 24 and ending at page 6, line 3 to read as follows:

(wherein “n’s in individual amino acid residues are the same or different, and represent 0 or 1; X¹, X⁸, X²⁷ and X²⁸ are the same or different, representing Leu or Ile; X² represents Asn or Lys; X³ represents Trp, Lys, Leu, Ala or Glu; X⁵ represents Ala or Ser; X⁶ represents Glu, Asp or Asn; X⁷ represents Val, Thr or Arg; X⁹ represents Lys, Asp, Ala or His; X²⁶ represents Gln, His, Gly, Asp or Asn; and X²⁹ represents Ala, Arg, Lys or Glu), and SEQ ID NO: 26, e.g., a sequence represented by the general formula (Ib);

Please amend the paragraph at page 6, lines 17-20 to read as follows:

The peptide sequence comprising a partial amino acid sequence having at least 12 continuous residues in the sequence of the DNA binding region of the E2F includes SEQ ID NO: 27, e.g. a sequence represented by the general formula (Ic);

Please amend the paragraph at page 24, lines 16-24 to read as follows (the changes are indicated in bold):

Into the XhoI- and HindIII sites of luciferase reporter vector pluc2 with neomycin (G418) resistant gene [Eur. J. Haematol., 52, 73 (1994)] were inserted an SphI-HindIII fragment composed of the 200 base pairs in the core promoter region of the SV40 initial gene **{128-0/5243-5171, base number according to “DNA Tumor Viruses, Tooze, J. Molecular Biology of Tumor Viruses, 2nd Ed., Part 2 Revised., Edited by J. Tooze DNA Tumor Viruses, Cold Spring Harbor Laboratory Press, 1982}**}, and a fragment produced by annealing the following two synthetic oligonucleotides;